REMARKS

Claims 7-29, 33-37, 43, 55, 56, 59-63, 67, 71-79, 81-87, 92-95, 117, 118, and 120-129 are currently pending.

Applicants respectfully request reconsideration in view of the following remarks and claim amendments. Issues raised in the Office Action will be addressed below in the order they appear in the Action.

Objection to the Specification

The Office Action objects to the specification for alleged non-compliance with the Sequence Rules.

Applicants submit herewith a corrected sequence listing to obviate this objection. Reconsideration and withdrawal of the objection are respectfully requested.

Objection to the Claims

Claims 7-29, 33-37, 43, 55-56, 59-63, 67, 71-79, 81-87, 92-95, 117-118, 120-129 are objected to because the claims allegedly do not comply with the Sequence Rules.

Applicants submit herewith a corrected sequence listing to obviate this objection. Reconsideration and withdrawal of the objection are respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 11, 18, 22-24, 26, 28, 33-36, 55, 56, 67, 71, 73, 121 and 123 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Viken *et al.* (*Human Immunology* **43**: 200-206, 1995, or "Viken").

Claims 11, 20, 22-24, 26, 28, 33-36, 55, 56, 61, 67, 73, and 78 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kolstad *et al.* (*Tissue Antigens* **31**: 90-97, 1988, or "Kolstad").

The Office Action alleges that both references disclose antibodies, which allegedly satisfy certain features of several *dependent* claims (such as Claims 20, 33-35, 55, 56, 61, 73, 78). However, the Office Action admits that neither reference specifically disclose the sequences of the antigen binding domains of the allegedly anticipating antibodies, or the epitopes to which they bind. Nevertheless, the Office Action argues that "the claimed antibodies appear to be the same as the prior art antibodies in term of human origin, target antigen and cytotoxicity to lymphoid cells, absent a showing of unobvious differences."

Based on this reasoning, the Office Action relies on *In re Best*, 562 F.2d 1252 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922 (PTO Bd. Pat. App. & Int. 1989) to shift the burden of proof to Applicants: "[t]he Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structure and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences."

Applicants respectfully disagree.

"It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986). To prove anticipation, one must show that "each element of the claim in issue is found, either expressly or under principles of inherency, in a single prior art reference" (emphasis added). *Minnesota Mining & Manufacturing Co. v. Johnson & Johnson Orthopedics, Inc.*, 976 F.2d 1559, 24 USPQ2d 1321 (Fed. Cir. 1992). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the

applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning tending to show inherency, the burden shifts to the Applicant to show an unobvious difference. "The PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on 'prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same..." *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)). The burden of proof is similar to that required with respect to product-by-process claims.

Here, all pending claims are directed to polypeptide compositions having specific recited amino acid sequences. To anticipate these claims, an alleged prior art reference must disclose each and every limitation of the claims, including the specific recited sequences, either expressly or under the principle of inherency. As the Examiner admits, neither of the cited references expressly disclose the recited sequences. Thus the rejections can only stand if anticipation can be proven under the principle of inherency. In other words, the Examiner must prove that the cited references disclose antibodies that necessarily comprise the recited VH and/or VL sequences.

Applicants submit that the Office Action has failed to show that the cited references necessarily comprise the recited VH and/or VL sequences. The only reason advanced by the Office Action in this regard is that "the claimed antibodies appear to be the same as the prior art antibodies in term of human origin, target antigen and cytotoxicity to lymphoid cells, absent a showing of unobvious differences." Essentially, the Office Action's reasoning amount to an argument that if a prior art human antibody binds to the same *antigen* (note: not *epitope*) bound by a claimed human antibody, and both antibodies appear to share one function (such as cytotoxicity), then both antibodies necessarily have the same antigen binding sequences.

Applicants submit that this argument fails for at least two reasons. First, as a skilled artisan will appreciate, monoclonal antibodies bind to an *epitope* on an *antigen*, which may have many distinct epitopes. Two monoclonal antibodies binding to the same multi-epitopic antigen, such as

HLA-DR8 0801 or HLA-DR52w in the cited references, may bind to completely different epitopes of the antigen. If so, these two monoclonal antibodies are almost certainly different in their variable (antigen-binding) region sequences. Second, even if two monoclonal antibodies happen to bind the same epitope, their variable (antigen-binding) region sequences are far from "necessarily identical," as is required under the inherency principle. Here, the Examiner admits that Viken does not specifically disclose the epitope to which the disclosed antibody binds. The Office Action does not point out, and Applicants are unable find where in Kolstad is the disclosure regarding the epitope to which the disclosed antibody binds. Thus the Examiner has failed to carry her burden to "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

Relying on two cases, the Office Action attempts to shift the burden of proof to Applicants. Applicants submit that the Office Action has misread the case law.

First of all, both cited cases (*In re Best* and *Ex parte Gray*) relate to product-by-process claims. "The Patent Office bears a lesser burden of proof in making out a case of *prima facie* obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. *In re Fessmann*, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). However, none of the pending claims in the instant application are product-by-process claims, in that all claims specifically recite defined amino acid sequences (structural features) and specific functional characteristics (functional features). In other words, the claimed polypeptide compositions are not claimed based on *how they are made*, but rather based on *what they are* and *what they do*. Thus the lesser burden of proof for such product-by-process claims does not apply in the instant situation.

Furthermore, *In re Best* has held that "if the claimed and prior art products are identical or substantially identical ... the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product" (emphasis added). *In re Best*, 562 F.2d 1252 (CCPA 1977). However, it has never held the other way around, *i.e.*, to allow the Office to shift the burden to Applicants to prove that the claimed and prior art products are not identical or substantially identical, merely because the PTO shows that the prior art products possess

substantially the same characteristics of his claimed product. Here, the Office Action attempts to do just the latter, despite its failure to show even that the prior art antibodies bind to the same epitopes as the claimed polypeptide compositions.

In conclusion, the Office Action has failed to show that the cited references disclose each and every element of the claimed invention. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102 are respectfully requested.

CONCLUSION

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. **18-1945**, from which the undersigned is authorized to draw under Order No. **GPCG-P01-003**.

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Respectfully submitted,

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